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Original article

Behavior of patients at high risk of developing contrast induced nephropathy after coronary procedures

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ARTICLE INFO

ABSTRACT

This study aimed to make a picture of patients at highest risk of developing contrast induced nephropathy (CIN) in order to take appropriate prevention measures. 591 patients undergoing coronary procedures were divided up into two groups: patients with (CIN-group) and without (no-CIN) an increase in creatinine level equal or more than 25% from baseline values within 24–48 h after the coronary procedure. All patients underwent an accurate anamnesis, objective exam, hematochemical measurements, and diagnostic exams. The results of this study one hand confirmed that, average age ($p = 0.01$), diabetes mellitus ($p < 0.0001$), kidney failure ($p = 0.0001$), diuretic therapy ($p = 0.002$), higher contrast doses ($p = 0.01$), are associated with a higher risk of contrast-induced nephropathy, on the other suggested that both clinical ($p = 0.01$) and subclinical ($p < 0.0001$) atherosclerosis, and higher preprocedural high sensitive C-reactive protein (hs-CRP) ($p = 0.02$) may more exposed to CIN.

1. Introduction

Contrast-induced nephropathy (CIN) is the third leading cause of hospital-acquired acute renal failure, accounting for 10% of all cases of hospital-acquired renal failure.[1] It is commonly defined as an acute deterioration of the renal function characterized by a significant increase in creatinine serum levels, usually more than 0.5 mg/dl (44 μmol/L) or 25% of baseline levels, within 24–48 h after exposure to a contrast agent compared to baseline serum creatinine values, when alternative explanations for renal impairment have been excluded.[2] The CIN represents an actual problem associated with increased mortality and morbidity and costs,[3–5] in fact, although usually transient, its resolution needs 1–3 weeks in average, the impairment of renal function may be permanent in some cases with the risk of progression towards chronic renal failure and the necessity of a temporary or lasting dialysis.[6] Prevention is the key to reduce the incidence of CIN and it begins with identification of the high risk patient coupled with appropriate peri-procedural management. Many studies have been conducted to identify the main risk factors for CIN, in fact many score systems have been proposed[7–12] and increasing number of guidelines have been suggested in literature[13,14] to help lessen the complication of CIN.

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A strong correlation was found between risk of CIN and pre-existing renal impairment, diabetes mellitus, advanced age, peri-procedural intravascular depletion, congestive heart failure, volume and type of contrast administered, and concomitant use of other nephrotoxic drug.[5,7,15] Few studies have, instead, investigated the role of systemic inflammation and extracardiac atherosclerosis as possible independent predictors of CIN. Some recent study found that elevated pre-procedural C-reactive protein (CRP) levels may be associated with an increased risk for CIN after percutaneous coronary intervention (PCI).[16,17]

The aim of this study was to make a picture of patients at highest risk of developing CIN after coronary angiography and/or percutaneous coronary intervention, in order to take appropriate prevention measures, analyzing the risk factor, evaluated extensively in the literature, and assessing if other factor, as marker of inflammation and atherosclerosis, may be considered independent predictor for CIN.

2. Material and methods

2.1. Study population

In our clinical experience we assessed a population composed of 1300 consecutive patients undergoing coronary angiography and, if necessary, elective or emergency percutaneous coronary intervention from October 2006 to June 2008 in Center for the Early Diagnosis of Preclinical and Multifocal Atherosclerosis and for the Secondary Prevention, University Hospital "P. Giaccone" of the University of Palermo—Italy. We excluded the patients admitted in other departments after procedures, making impossible to monitor their clinical conditions and to perform hematochemical surveys, in pregnancy, underwent coronary artery by pass graft (CABG) within 48 of coronary angioplasty, with many different causes which had avoided the evaluation of CRP levels and creatinine serum level at admission, with life expectancy <1 year. Patients were also excluded if they had concomitant inflammatory conditions (such as active infection, inflammatory arthritis or connective tissue disease) or malignancies or had recent (<4 months) surgery or major trauma.

In this manner, a final sample size of 591 (45.46%) of 1300 patients were enrolled and underwent an accurate anamnesis, objective exam, haematochemical measurements, the ultrasonography of carotid arteries and ankle-brachial pressure index (ABI) measurements.

The database compiled for each patient contains the data listed in Table 1.

Family history of CAD (Coronary artery disease) was defined as a coronary event occurring before 55 and 65 years, for first-degree male and female, respectively. Diabetes mellitus was defined as a fasting glucose ≥126 mg/dl on at least two separate occasions or as the use hypoglycemic drugs.[18] Hypertension was defined as a blood pressure >140/90 mmHg or as use antihypertensive drugs. Present smokers if they were current smokers or had stopped since less than 1 year. Obesity was defined as a body max index ≥30 kg/m². Anemia was defined as hemoglobin level less than 13 g/dl in men and less than 12 g/dl in women.[19] Dyslipidemia defined as plasma triglycerides >150 mg/dL and/or plasma low-density lipoprotein cholesterol (LDL-C) >130 mg/dL and or plasma (high-density lipoprotein-cholesterol) HDL-C <40 mg/dL in men and <50 mg/dL in women. Multivessel CAD was defined as two or more lesion (>50%) in different epicardial coronary arteries.

The presence of extracoronary atherosclerosis we demonstrated by echo-color Doppler exams and measurement of ABI (Ankle Brachial Pressure) performed before or during stay in hospital, taking into account any site: carotid vessels and inferior limbs. In our study we considered the term of extracoronary atherosclerosis both clinical atherosclerosis and preclinical atherosclerosis.

Chronic Renal Insufficiency (CRI), assessed at admission, was defined as an estimated Glomerular Filtration Rate (eGFR) below 60 mL/min/1.73 m and calculated using a modified MDRD equation.

All patients were closely monitored during their stay in hospital to assess their creatinine serum peak 3—4 days after contrast procedure: if subjects were discharged earlier, they were invited to undergo a blood sample privately and to transmit us their results. Two groups of patients were individualized in the study population: age according to percentage variation of serum creatinine between the pre and the post procedural phase: "CIN-group" and "no-CIN group".

CIN was defined as an absolute increase in serum creatinine of 25% from baseline values occurring within 24—48 h after the coronary procedure.[2]

2.2. Biochemistry

A blood sample was drawn in the morning, before the medical examination, after a 12—14 h overnight fast Total cholesterol (TC), triglycerides (TG), and HDL-cholesterol were quantified by standard enzymatic-colorimetric methods[20] and LDL-cholesterol was calculated by Friedewald's method.

The patients had blood drawn for hs-CRP analysis immediately before primary coronary intervention.

High sensitive (hs)-CRP was determined by the nephelometric method (Beckman Instrument APS).[21]

Fibrinogen determination was rapidly performed according to the coagulative method of Clauss.[22]

2.3. Echocolordoppler examination of carotid arteries

B-mode real-time ultrasound (Toshiba 270 SS) was performed to evaluate the arterial wall thickness in the carotid arteries using a probe of 7.5—10.0 MHz. As already reported[23,24] patients were examined in the supine position and each carotid wall or segment was examined to identify the thickest intimal-medial site. Each scan of the common carotid artery began just above the clavicle, and the transducer was moved until the carotid bifurcation and along the internal carotid artery. Three segments were identified and measured in antero and posterior planes on each side: the distal 1.0 cm of the common carotid proximal to the bifurcation, the bifurcation itself, and the proximal 1.0 cm of the internal carotid artery. At each of these sites we detected any possible plaque and determined the IMT as defined as the distance between

Table 1 – Main characteristics between "CIN-group" and "no-CIN group". Results of univariate analysis.

	No-CIN (n = 486)	CIN (n = 105)	p value <0.05
Demographic characteristics			
Mean age	65.32 ± 12.02	68.94 ± 11.31	0.004
Male n (%)	69.3% (337)	69 (65.7)	0.54
Clinical characteristics n (%)			
Diabetes mellitus	150 (30.9%)	44 (42%)	0.03
Smoke	141 (29.0%)	30 (28.6%)	0.97
Ex smoke	132 (27.2%)	22 (20.9%)	0.23
Dyslipidemia	233 (47.9%)	53 (50.5%)	0.72
Family history	189 (38.9%)	45 (42.8%)	0.51
Arterial hypertension	340 (69.9%)	83 (80.0%)	0.05
Anemia	50 (10.3%)	19 (18.1%)	0.03
Previous CRI	61 (12.5%)	28 (26.6%)	<0.001
Obesity (BMI >30 kg/m^2)	72 (14.8%)	23 (21.9%)	0.09
Previous CABG	39 (8.0%)	14 (13.3%)	0.12
Previous IMA	138 (28.4%)	33 (31.4%)	0.61
Previous AF	42 (8.6%)	9 (8.6%)	0.86
Previous PCI	130 (26.7%)	23 (21.9%)	0.36
Previous HF	24 (4.9%)	7 (6.7%)	0.63
Valvular disease	36 (7.4%)	3 (2.8%)	0.13
Thyroid disease	32 (6.6%)	4 (3.8%)	0.39
Diabetic complication	18 (3.7%)	2 (1.9%)	0.53
Thromboembolic disease	1.0% (5)	2 (1.9%)	0.79
Biological characteristics			
Total cholesterol (mg/dl)	171.52 ± 44.12	168.7 ± 41.56	0.56
HDL cholesterol (mg/dl)	43.26 ± 11.89	41.68 ± 12.86	0.22
LDL cholesterol (mg/dl)	100 ± 38.09	104.29 ± 37.73	0.29
Triglycerides (mg/dl)	134.24 ± 73.03	135.79 ± 79.50	0.85
Inflammatory markers			
Hs-CRP (mg/L)	1.63 ± 5.5	2.84 ± 4.27	0.03
ESR (mm/h)	17.36 ± 16.67	28.94 ± 21.14	<0.001
Fibrinogen (mg/dl)	368.42 ± 98.15	394.91 ± 113.99	0.02
Diagnosis extracoronary ATS n (%)	215 (44.2%)	68 (64.8%)	<0.001
Clinical ATS n (%)	148 (30.4%)	44 (41.9%)	0.03
Preclinica ATS n (%)	67 (13.8%)	24 (22.9%)	0.02
Medications n (%)			
Diuretics	106 (21.8%)	37 (35.2%)	0.005
Ace-inhibitors	253 (52.1%)	61 (58.1%)	0.31
Sartans	114 (23.4%)	24 (22.8%)	0.99
Statins	366 (75.3%)	85 (80.9%)	0.26
NSAIDS	414 (85.2%)	90 (85.7%)	0.98
Angiography characteristics			
Emergency procedure n (%)	66 (11.16%)	30 (28.6%)	<0.001
Bare metal stent n (%)	263 (54.11%)	58 (55.23)	0.91
N°stents	1.44 ± 0.60	1.45 ± 0.55	0.87
Type of contrast media n (%)			
Iodixanol (Visipaque)	320 (65.8%)	71 (67.6%)	0.81
Iomeprol (Iomeron)	94 (19.3%)	20 (19.0%)	0.94
Ioversol (Optiray)	72 (14.8%)	14 (13.3%)	0.81
Mean doses of contrast media (cc)	115.1 ± 83.56	136.9 ± 101.73	0.02
Multivessel disease n (%)	200 (41.15%)	45 (42.85)	0.83
0 sick vessels n (%)	115 (23.6%)	18 (17.1%)	0.18
1 sick vessel n (%)	151 (31.0%)	35 (33.3%)	0.73
2 sick vessels n (%)	108 (22.2%)	20 (19%)	0.55
3 sick vessels n (%)	100 (20.6%)	27 (25.7%)	0.29
Common trunk n (%)	28 (5.8%)	10 (1.7%)	0.13

CRI, chronic renal insufficiency; CABG, coronary artery by pass graft; IMA, acute myocardial infarction; AF, atrial fibrillation; PCI, percutaneous coronary intervention; HF, heart failure; HDL, high density lipoprotein; LDL, low density lipoprotein; hs-CRP, high sensitivity C reactive protein; ESR: erythrocyte sedimentation rate; ATS, atherosclerosis; ACE, angiotensin converting enzyme; NSAIDs non steroidal anti-inflammatory drugs.

the echogenic line representing the intima blood interface and the outer echogenic line representing the adventitia junction.

Subjects with subclinical carotid atherosclerosis were considered, in accordance to the joint ESH/ESC guidelines, in relation to the ultrasound report, both subject with intima-media thickening (with IMT >0.9 mm and <1.5 mm) and subjects with asymptomatic carotid plaque (APC) (IMT >1.5 mm).[25]

2.4. Ankle-brachial index measurement

Measurement of Ankle-Brachial Index (ABI) is an easy-to-perform, inexpensive, reproducible and non-invasive test.[19] It was performed with the patient supine; systolic blood pressure was recorded at both arms and both ankles with an Esaote Caris Plus ultrasound scanner using a 7.5−10.0 MHz linear probe.

ABI was calculated for each leg by diving the highest ankle pressure by highest pressure of both arms. An ABI <0.90 is widely accepted as a reasonable cut point to confirm the diagnosis of preclinical atherosclerosis of arteries supplying the legs.[26]

2.5. Statistical analysis

Continuous variables were presented as mean ± SD and compared using Student's t test. In case of non normal distribution, non parametric methods were used (Mann−Whitney U test). Categorical variables were presented as counts and percentages and compared with χ^2-test when appropriate (expected frequency >5). Otherwise, Fisher's exact test was used. p value <0.05 was considered statistically significant. To identify independent characteristics associated with CIN multivariable logistic regression analysis was used. Results of this model were presented as Odds Ratio (OR) and 95% confidence intervals (95% CI) for OR. Models were developed with stepwise techniques and by consideration of potential confounding factors and of variables that are shown to be statistically significant at univariate analysis. All data was processed using MedCalc software version 11.3.0.0.

3. Results

The study population consisted of 591 patients with a mean age 65.96 ± 11.31 years, 406 (68.69%) were men.

The patient sample was divided up into 2 groups: "CIN-group" and "no-CIN group".

The "no-CIN group" included a total of 486 patients, 337 males (69.3%) and 149 females (30.7%) with average age 65.32 ± 12.02 years [Table 1].

The CIN group included a total of 105, 69 males (65.7%) and 36 females (34.3%) with average age 68.94 ± 11.31 years [Table 1].

The main clinical characteristics of the patient population are summarized in Table 1.

After univariate analysis, by analyzing different features, the CIN and no-CIN groups resulted to be fully homogeneous for the characteristics reported in Table 1 ($p > 0.05$).

On the contrary, as reported in Table 1, it emerged that patients of CIN group were older individuals than controls (68.94 ± 11.31 versus 65.32 ± 12.02 years, respectively; $p = 0.004$) and had significantly higher proportion of diabetes ($p = 0.03$), renal insufficiency ($p < 0.001$), emergency procedure ($p < 0.001$), therapy with diuretics ($p = 0.005$), anemia ($p = 0.03$) compared with patients of "no-CIN group", while arterial blood pressure was limit of significance ($p = 0.05$).

As regards cardiology procedures, in subjects who developed CIN a higher dose of contrast media was administered ($p = 0.02$), while the compared analysis of the patient groups in relation to the molecule type chosen to make coronaries opaque (iodixanol, iomeprol, ioversol), did not show any significant statistical difference.

An interesting relationship was found between systemic inflammation and extent of coronary atherosclerosis: an increase in blood levels of hs-CRP and fibrinogen, corresponded to a proportional increase in the number of diseased vessels [Figs. 1 and 2], this result could suggest a possible direct connection between this latest data and risk CIN, but this correlation is not statistically confirmed in univariate analysis (multivessel disease $p = 0.83$; 2 sick vessels $p = 0.55$; 3 sick vessels $p = 0.29$) [Table 1].

Moreover a statistically significant difference was found between the two groups for preprocedural CRP levels ($p = 0.03$), serum fibrinogen levels ($p = 0.015$) and erythrocyte sedimentation rate (ESR) ($p < 0.001$), particularly an increase of blood levels of hs-CRP corresponded to a proportional increase of CIN [Fig. 3].

Another important finding is that the Atherosclerosis Extracoronary both clinical ($p = 0.03$) and preclinical ($p = 0.02$) was more represented in the CIN group.

After we made a multivariate analysis to identify independent factor associated with contrast induced nephropathy, considering the variables that univariate analysis showed statistically significant difference (diabetes, diuretics, mean doses of contrast media, anemia, emergency procedure, inflammatory markers, extracoronary atherosclerosis, chronic renal insufficiency) and the potential confounding factors such as multivessel disease, sex, hypertension, type of contrast media, number of stent. From the logistic regression analysis age (OR = 1.03; 95%CI 1.01 to 1.05; $p = 0.01$), diabetes mellitus (OR = 3.04; 95%CI 1.81 to 5.10; $p = <0.0001$), treatment with diuretic (OR = 1.04; 95%CI 1.02 to 1.07; $p = 0.002$), dose of contrast (OR = 1.84; 95%CI 1.14 to 2.99; $p = 0.01$); CRP serum levels (OR = 1.92; 95%CI 1.10 to 3.36; $p = 0.02$), extracoronary atherosclerosis both clinical (OR = 1.84; 95%CI 1,16 to 2.94; $p = 0.010$) preclinical atherosclerosis (OR = 4.10; 95%CI 2.19 to 7.70; $p = <0.0001$) and previous chronic renal insufficiency (CRI) (OR = 2.77; 95%CI 1.67 to 4.60; $p = 0.0001$), were independent predictors of the CIN [Table 2].
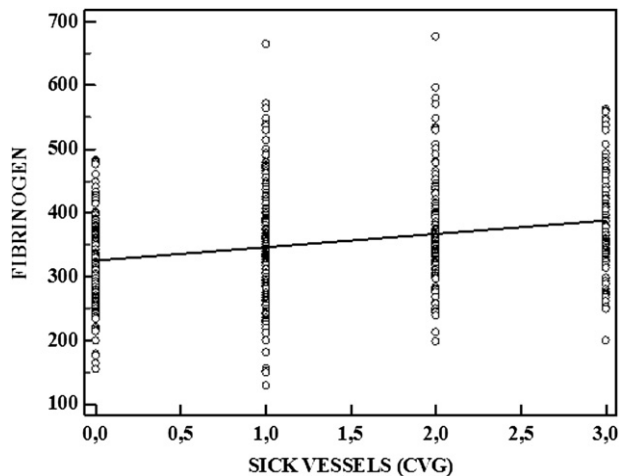
Fig. 1 − Linear relationship between fibrinogen serum levels and number of sick vessels.
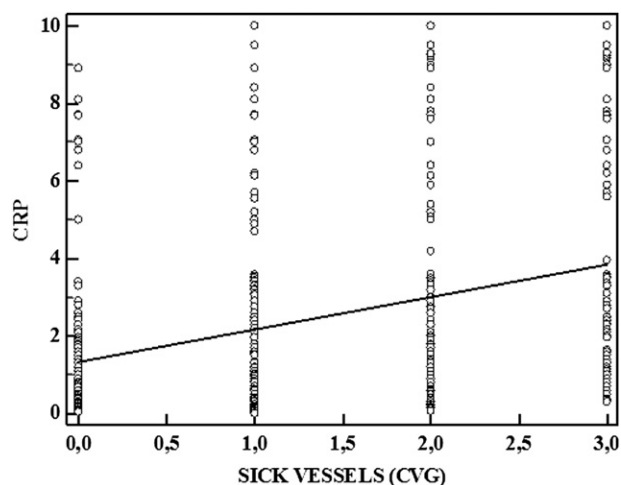
Fig. 2 — Linear relationship between hs-CRP serum levels and number of sick vessels.

4. Discussion

Contrast induced nephropathy (CIN) is a feared complication of radiological procedures that expose patients to contrast media. Although the risk of renal function impairment associated with radiologic procedures is low in the general population, it may be very high in selected patient subsets, especially in cardiac procedures[6,15,27] such as percutaneous coronary intervention (PCI) and coronary angiography. Not only is this a leading cause of morbidity and mortality, but it also adds to increased costs in high risk patients undergoing percutaneous coronary intervention.

In our clinical experience we evaluated a patient population, dividing it into two arms according to the onset of contrast induced nephropathy after coronarography and/or percutaneous angioplasty.

By statistical analysis of baseline characteristics of study population, some peculiar factors seemed to be strongly correlated to the risk of developing CIN.
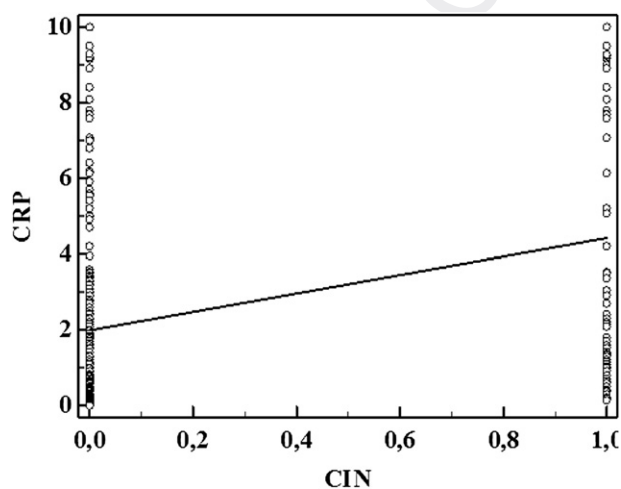

Fig. 3 — Linear relationship between hs-CRP serum levels and CIN (contrast induced nephropathy).

Table 2 — Independent correlates of CIN.			
		95% CI	
	OR	Lower	Upper	p value
Age	1.03	1.01	1.05	0.01
Diabetes mellitus	3.04	1.81	5.10	<0.0001
Diuretics	1.04	1.02	1.07	0.002
Mean doses of contrast media (cc)	1.84	1.14	2.99	0.01
Hs-CRP (mg/L)	1.93	1.10	3.36	0.02
Diagnosis extracoronary ATS				
Clinical ATS	1.85	1.16	2.94	0.01
Preclinical ATS	4.11	2.19	7.70	<0.0001
Previous CRI	2.77	1.67	4.60	0.0001

Hs-CRP, high sensitivity C reactive protein; ESR: erythrocyte sedimentation rate; ATS, atherosclerosis; CRI, chronic renal insufficiency.

The incidence of CIN is considerably higher in elderly patients, in patients affected by diabetes mellitus, kidney failure, undergoing diuretic therapy, treated with higher contrast doses than the general population, according to literature data[5,7,15,28] and in patients with a state of systemic inflammation and extra cardiac atherosclerosis both clinical and preclinical. The elderly remain at a higher risk of CIN after PCI, a few studies have found age older than 70 years to be an independent predictor of CIN in multivariate analysis.[29] Mehran et al, similarly, found eight variables for patients who underwent PCI (hypotension, intra-aortic balloon pump, congestive heart failure, chronic kidney disease, diabetes, age 75 years, anemia, and volume of contrast) and assigned a weighted integer to each variable to make up a score cumulatively so as to divide low risk (5) and high risk (16) scores.[7] Many studies have found Diabetes Mellitus (DM) as an independent risk factor for CIN.[5,15,30] Toprak et al showed that in patients with preexisting renal insufficiency, Diabetes Mellitus independently increased the risk of development of CIN and need for dialysis as opposed to pre-DM and Normal Fasting states,[31] while Berns showed that the incidence of CIN in diabetics was higher if Cr 4.0 compared to Cr between 2.0 and 4.0 mg/dL. Clearly, there is a synergistic effect of diabetes and pre existing renal insufficiency.[32]

As expected, the presence of a previous renal insufficiency, defined as an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2, turned out a very sensitive index of CIN.[6,33] Based on the available evidence in the literature the risk of CIN is inversely related to the calculated estimated GFR (eGFR).[15]

Studies have shown that diuretics and mannitol have no beneficial effects and may be harmful[34,35] and their use cannot be recommended for CIN prophylaxis. In fact the use of loop diuretics may actually exacerbate post-procedural renal function.[36] On the other hand preprocedure hydration seems to be the best strategy for preventing CIN.[13—37]

Our data showed that the CIN risk increases proportionally to the doses of contrast media. Intuitively, the less contrast media administered, the lower the risk for CIN, in fact volume of contrast remains the primary modifiable risk factor.[38] Many studies have documented a clear correlation between volume

of contrast and risk of CIN.[38,39] However, whether incidence of CIN is dose related or not has also been studied. In their study, Mekan et al found that the contrast-induced reduction in renal function was not significantly higher with a higher volume of contrast (100 mL).[40] On the other hand, Kane et al demonstrated a significant rise in incidence of CIN with increase of volume of contrast.[38] Although the pathogenesis of this condition is not fully understood, it is most likely the result of the prolonged vasoconstriction, for alterations in nitric oxide metabolism that lead to renal vasoconstriction, and impaired autoregulation induced by contrast media predisposing to medullary hypoxia, in combination with direct cytotoxicity to the renal tubular epithelium. This may be further influenced by contributions from several systemic factors, in fact the damage may be mediated by formation of free radicals in the acidic tubular environment.[41] Therefore, an appreciation of the factors affecting renal microcirculatory hemodynamics is pivotal to understanding the pathogenesis of CIN and the expected response to preventive measures.

In particular, the hemodynamic theory of CIN pathophysiology would be indirectly confirmed by another datum we found, that is, the higher predisposition to CIN occurrence in subjects undergoing emergency CVG or PCI. In fact contrast-induced nephropathy frequently complicates primary PCI, even in patients with normal renal function.[42] Actually, the acute cardiocirculatory failure of these patients could cause a contrast-induced damage both by worsening kidney hypoperfusion and by preventing to take appropriate preventive measures before intervention. The type of molecule used as contrast media was not a differential factor between the two groups: this is easy understandable considering that in our hemodynamic laboratory only low-osmolar non ionic monomers or iso-osmolar ionic and non-ionic dimers are used, in accordance with the latest evidences on the least dangerous molecules for the kidney.[43,44]

Another very interesting aspect that came up from our study concerns the role of systemic inflammation.

Although at multivariate analysis, the fibrinogen levels and erythrocyte sedimentation rate (ESR) were not independent predictors, elevated pre-procedural C-reactive protein provide a strong and independent predictor of CIN.

Recent studies have reached similar results, despite few studies have investigated hs-CRP as a risk factor for contrast-induced nephropathy. Gao et al in their study demonstrated that elevated preprocedural CRP was associated with an increased risk for CIN in patients undergoing PCI.[16] Lyu et al showed that CRP was a significant and independent predictor of CIN after primary PCI in patients with STEMI.[17] Some studies indicated that the administration of statins was associated with reduced incidence of CIN in patients undergoing PCI and the beneficial effect of statins on systematic inflammation and endothelium dysfunction has been well documented.[45,46]

Furthermore, when the degree of systemic inflammation increased, the number of sick vessels increased too, confirming a trend of recent evidences linking hs-CRP to atherosclerotic disease.[47,48] On the basis of these results, we wondered if there was also a direct relationship between the number of sick vessels and the CIN risk, but this datum was not statistically proved. Moreover, despite the fact that no firm conclusions can be drawn at this stage, it was emerged from our study as extracoronary atherosclerosis both preclinical and clinical, may be another strongly predictive index of CIN after PCI and this could confirm the hypothesis, made by some authors,[49] that atherosclerosis is the actual link between cardiovascular and renal diseases, even considering the worse cardiovascular outcome of patients who develop CIN.[10,50] In fact, the systemic inflammatory process, of which atherosclerosis is an expression, may induce alterations in the renal microcirculation, predisposing to CIN. Especially to emphasize its role as independent factor of preclinical atherosclerosis valued at carotid and lower limbs, in fact, although the total number of patients with atherosclerosis preclinical in the two groups is very small, the role of preclinical atherosclerosis, as predictor of CIN, should not be underestimated: the preclinical atherosclerosis, if left to its free evolution, in fact, in addition to the known cardiac complications, may lead to an increased susceptibility to CIN. It follows that IMT and ABI if properly interpreted, becomes an early indicator of damage.

An interesting fact was that after a multivariate analysis, anemia was not a risk factor, contrary to previous studies,[7−9] probably because of the small percentage of subjects with anemia in the population.

Our study has some limitations: the study included a small population, admitted to a single center, due to limited availability of data fields, we could not consider periprocedural hydration volume, proteinuria, urine output, intra-aortic balloon pump in our multivariate analysis. In our institution, prophylactic use of sodium bicarbonate or N-acetylcisteine infusion is extremely rare due to their conflicting clinical results, so it was available for our analyses. In addition the impossibility to conclude causality or exclude unmeasured confounding as a contributor to the observed association, we cannot exclude the presence of a selection bias and the possibility that other factors, might have contributed, at least in part, to renal impairment, and influenced the clinical outcome of our patients.

5.   Conclusions

The findings of this study on one hand, according to literature data, provides further epidemiological evidence that, diabetes mellitus, volume of contrast media, diuretics, kidney failure are associated with a higher risk of contrast-induced nephropathy, on the other suggest that patient with high levels of CRP and extra cardiac atherosclerosis may be more exposed to CIN. It follows that IMT, ABI and above all, preprocedural CRP level if properly interpreted, becomes an early indicator of CIN.

Pending further studies to confirm these results, in light of these data, it would be important to be able to better define the role of both preprocedural CRP level and atherosclerosis with respect CIN and to assess if preprocedural risk stratification with these factors as an adjunct to established clinical risk factors, further confirmed in our study, may be useful as form of prevention for early identification of high risk patients for CIN. Research now in progress will almost certainly help clarify the picture.

Conflicts of interest

All authors have none to declare.

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